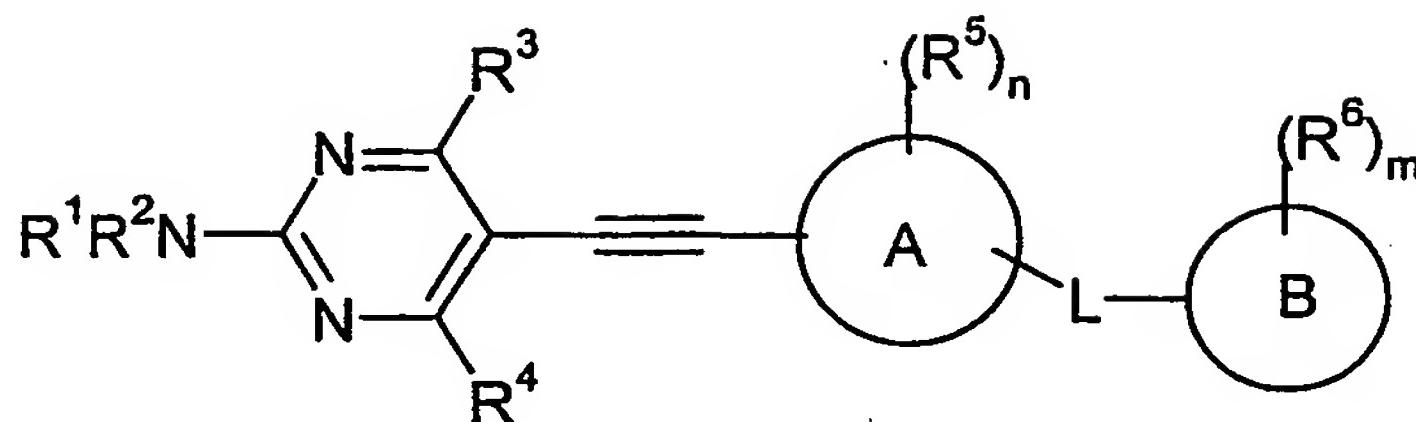


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**CLAIMS**

1. A compound of the Formula I:



5

Formula I

wherein:

**R<sup>1</sup>** and **R<sup>2</sup>** are independently selected from hydrogen, (1-6C)alkylsulfonyl, phenyl(CH<sub>2</sub>)<sub>u</sub>- wherein u is 0, 1, 2, 3, 4, 5 or 6, (1-6C)alkanoyl, (1-6C)alkyl, (1-6C)alkoxycarbonyl, (3-6C)cycloalkyl(CH<sub>2</sub>)<sub>x</sub>- in which x is 0, 1, 2, 3, 4, 5 or 6, or a 5 or 6 membered heteroaryl ring, or **R<sup>1</sup>** and **R<sup>2</sup>** together with the nitrogen atom to which they are attached represent a saturated or partially saturated 3 to 7 membered heterocyclic ring optionally containing another hetero atom selected from N or O;

10  
wherein the (1-6C)alkyl, the (1-6C)alkanoyl and the (3-6C)cycloalkyl groups are optionally substituted by one or more groups independently selected from

15  
fluoro, hydroxy, (1-6C)alkyl, (1-6C)alkoxy, (1-6C)alkoxy(1-6C)alkoxy, (1-6C)alkoxy(1-6C)alkoxy(1-6C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, carbamoyl, mono(1-6C)alkylcarbamoyl, di-[(1-6C)alkyl]carbamoyl, -N(R<sup>d</sup>)C(O)(1-6C)alkyl in which R<sup>d</sup> is hydrogen or (1-6C)alkyl, a saturated or partially saturated 3 to 7 membered heterocyclic ring, or a 5 or 6 membered heteroaryl ring,

20  
wherein the (1-6C)alkoxy, (1-6C)alkoxy(1-6C)alkoxy and (1-6C)alkoxy(1-6C)alkoxy(1-6C)alkoxy groups and the (1-6C)alkyl groups of the mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, mono(1-6C)alkylcarbamoyl, di-[(1-6C)alkyl]carbamoyl and/or -N(R<sup>d</sup>)C(O)(1-6C)alkyl groups are optionally substituted by one or more hydroxy groups;

25  
wherein the phenyl is optionally substituted by one or more groups independently selected from halo, (1-6C)alkyl, (1-6C)alkoxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino, wherein the (1-6C)alkyl and the (1-6C)alkoxy

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groups are optionally substituted by one or more groups independently selected from hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino; and wherein any heterocyclic and heteroaryl rings within R<sup>1</sup> and/or R<sup>2</sup> are optionally independently substituted by one or more of the following:

5 (1-4C)alkyl, (1-4C)alkoxy, (1-4C)alkoxy(1-4C)alkyl, hydroxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, a saturated or partially saturated 3 to 7 membered heterocyclic ring or -C(O)(CH<sub>2</sub>)<sub>z</sub>Y wherein z is 0, 1, 2 or 3 and Y is selected from hydrogen, hydroxy, (1-4C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino or a saturated or partially 10 saturated 3 to 7 membered heterocyclic ring;  
and provided that when R<sup>1</sup> and/or R<sup>2</sup> is a (1C)alkanoyl group, then the (1C)alkanoyl is not substituted by fluoro or hydroxy;

15 R<sup>3</sup> and R<sup>4</sup> are independently selected from hydrogen, (1-6C)alkyl or (1-6C)alkoxy, wherein the (1-6C)alkyl and the (1-6C)alkoxy groups are optionally substituted by one or more groups independently selected from: fluoro, hydroxy, (1-6C)alkyl, (1-6C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, carbamoyl, mono(1-6C)alkylcarbamoyl or di-[(1-6C)alkyl]carbamoyl, a saturated or partially saturated 3 to 7 membered heterocyclic ring or a 5 or 6 20 membered heteroaryl ring, wherein said heterocyclic and heteroaryl rings are optionally independently substituted by one or more of the following: (1-4C)alkyl, (1-4C)alkoxy, hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino or a saturated or partially saturated 3 to 7 membered heterocyclic ring;  
25 or one of R<sup>3</sup> and R<sup>4</sup> is as defined above and the other represents a group -NR<sup>1</sup>R<sup>2</sup> as defined above;

30 A represents an aryl group or a 5 or 6 membered heteroaryl ring selected from furyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl or 1,3,5-triazinyl;

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**R<sup>5</sup>** is selected from cyclopropyl, cyano, halo, (1-6C)alkoxy or (1-6C)alkyl, wherein the (1-6C)alkyl and the (1-6C)alkoxy groups are optionally substituted by cyano or by one or more fluoro;

5       **n** is 0, 1, 2 or 3;

10      **L** is attached meta or para on ring A with respect to the point of attachment of the ethynyl group and represents -C(R<sup>a</sup>R<sup>b</sup>)C(O)N(R<sup>9</sup>)-, -N(R<sup>8</sup>)C(O)C(R<sup>a</sup>R<sup>b</sup>)-, -N(R<sup>8</sup>)C(O)N(R<sup>9</sup>)-, -N(R<sup>8</sup>)C(O)O-, or -OC(O)-N(R<sup>9</sup>)-, wherein R<sup>8</sup> and R<sup>9</sup> independently represent hydrogen or (1-6C)alkyl and wherein R<sup>a</sup> and R<sup>b</sup> independently represent hydrogen or (1-6C)alkyl or R<sup>a</sup> and R<sup>b</sup> together with the carbon atom to which they are attached represent (3-6C)cycloalkyl;

15      **B** represents a (3-7C)cycloalkyl ring, a saturated or partially saturated 3 to 7 membered heterocyclic ring, an aryl group, a 5 or 6 membered heteroaryl ring selected from furyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl or 1,3,5-triazinyl, or a 8, 9 or 10 membered bicyclic group which optionally contains 1, 2, 3 or 4 heteroatoms independently selected from N, O and S and which is saturated, partially saturated or aromatic;

20      **R<sup>6</sup>** is selected from halo, cyano, oxo, a (3-7C)cycloalkyl ring, a saturated or partially saturated 3 to 7 membered heterocyclic ring, and -N(R<sup>c</sup>)C(O)(1-6C)alkyl in which R<sup>c</sup> is hydrogen or (1-6C)alkyl; or  
25      **R<sup>6</sup>** is selected from (1-6C)alkyl, -S(O)<sub>p</sub>-(1-6C)alkyl wherein p is 0, 1 or 2, or (1-6C)alkoxy, wherein the (1-6C)alkyl, -S(O)<sub>p</sub>-(1-6C)alkyl and the (1-6C)alkoxy groups are optionally substituted by one or more groups independently selected from cyano, fluoro, hydroxy, (1-6C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, a (3-7C)cycloalkyl ring or a saturated or partially saturated 3 to 7 membered heterocyclic ring; and

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wherein the (3-7C)cycloalkyl ring and saturated or partially saturated 3 to 7 membered heterocyclic ring are optionally independently substituted by one or more groups selected from (1-6C)alkyl; and

5       m is 0, 1, 2 or 3;

and when B is a (3-7C)cycloalkyl ring, a saturated or partially saturated 3 to 7 membered heterocyclic ring or a saturated or partially saturated 8, 9 or 10 membered bicyclic group, the rings and the bicyclic group optionally bear 1 or 2 oxo or thioxo  
10       substituents;  
and salts thereof.

2. A compound of Formula I according to Claim 1, wherein:

R<sup>6</sup> is selected from halo, cyano, a (3-7C)cycloalkyl ring, a saturated or partially  
15       saturated 3 to 7 membered heterocyclic ring or an alkanoylamino group  
-N(R<sup>c</sup>)C(O)(1-6C)alkyl in which R<sup>c</sup> is hydrogen or (1-6C)alkyl; or  
R<sup>6</sup> is selected from (1-6C)alkyl or (1-6C)alkoxy, wherein the (1-6C)alkyl and the  
20       (1-6C)alkoxy groups are optionally substituted by one or more groups independently  
selected from cyano, fluoro, hydroxy, (1-6C)alkoxy, amino, mono(1-6C)alkylamino,  
di-[(1-6C)alkyl]amino, a (3-7C)cycloalkyl ring or a saturated or partially saturated 3  
to 7 membered heterocyclic ring;  
and salts thereof.

3. A compound of the Formula I according to claim 1, wherein:

25       R<sup>1</sup> and R<sup>2</sup> are independently selected from hydrogen, (1-6C)alkylsulfonyl,  
phenyl(CH<sub>2</sub>)<sub>u</sub>- wherein u is 0, 1, 2, 3, 4, 5 or 6, (1-6C)alkanoyl, (1-6C)alkyl,  
(1-6C)alkoxycarbonyl, or (3-6C)cycloalkyl(CH<sub>2</sub>)<sub>x</sub>- in which x is 0, 1, 2, 3, 4, 5 or 6  
or R<sup>1</sup> and R<sup>2</sup> together with the nitrogen atom to which they are attached represent a  
30       saturated or partially saturated 3 to 7 membered heterocyclic ring optionally  
containing another hetero atom selected from N or O;  
wherein the alkyl and the cycloalkyl groups are optionally substituted by one or  
more groups selected from fluoro, hydroxy, (1-6C)alkyl, (1-6C)alkoxy, amino,  
mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino, a saturated or partially

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saturated 3 to 7 membered heterocyclic ring or a 5 or 6 membered heteroaryl ring, wherein said heterocyclic and heteroaryl rings are optionally independently substituted by one or more of the following: (1-4C)alkyl, hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino or a  
5 saturated or partially saturated 3 to 7 membered heterocyclic ring;

and wherein the phenyl is optionally substituted by one or more groups selected from halo, (1-6C)alkyl, (1-6C)alkoxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino, wherein the (1-6C)alkyl or (1-6C)alkoxy are optionally substituted by hydroxy, amino, mono(1-6C)alkylamino or  
10 di-[(1-6C)alkyl]amino;

15 **R<sup>3</sup>** and **R<sup>4</sup>** are independently selected from hydrogen, (1-6C)alkyl or (1-6C)alkoxy wherein the alkyl and the alkoxy groups are optionally substituted by one or more groups selected from fluoro, hydroxy, (1-6C)alkyl, (1-6C)alkoxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino, a saturated or partially saturated 3 to 7 membered heterocyclic ring or a 5 or 6 membered heteroaryl ring, wherein said heterocyclic and heteroaryl rings are optionally independently substituted by one or more of the following: (1-4C)alkyl, hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino or a saturated or partially saturated 3 to 7 membered  
20 heterocyclic ring;

or one of **R<sup>3</sup>** and **R<sup>4</sup>** is as defined above and the other represents a group  $-NR^1R^2$  as defined above;

25 **R<sup>5</sup>** is selected from cyano, halo, (1-6C)alkoxy or (1-6C)alkyl optionally substituted by cyano or by one or more fluoro;

30 **B** represents a (3-7C)cycloalkyl ring, an aryl or a 5 or 6 membered heteroaryl ring selected from furyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl or 1,3,5-triazinyl;

**R<sup>6</sup>** is selected from halo, cyano, a saturated or partially saturated 3 to 7 membered heterocyclic ring or an alkanoylamino group  $-N(R^c)C(O)(1-6C)alkyl$  in which **R<sup>c</sup>** is

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hydrogen or (1-6C)alkyl; or R<sup>6</sup> is selected from (1-6C)alkyl or (1-6C)alkoxy, wherein the alkyl and the alkoxy groups are optionally substituted by one or more groups selected from cyano, fluoro, hydroxy, (1-6C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, or a saturated or partially saturated 5 3 to 7 membered heterocyclic ring; and

m is 0, 1, 2 or 3; and when m is at least 2 then two substituents on adjacent carbon atoms in ring B may together represent a methylenedioxy group;

10 and wherein A, L and n are as defined in Claim 1.

and salts thereof.

4. A compound according to any one of Claims 1, 2 and 3 wherein A is selected from phenyl, pyridyl, thiazolyl, thiadiazolyl or pyrimidinyl.

15

5. A compound accordingly to any one of the preceding claims wherein B is selected from phenyl, 2,3-di-hydro-indenyl, piperidinyl, pyridyl, pyrazolyl, isothiazolyl, thiadiazolyl, isoxazolyl, benzodioxinyl, benzodioxolyl or tetrahydropyranyl

20 6. A compound accordingly to any one of the preceding claims wherein L is selected from -N(R<sup>8</sup>)C(O)N(R<sup>9</sup>)-, -N(R<sup>8</sup>)C(O)O- or -N(R<sup>8</sup>)C(O)CH<sub>2</sub>- wherein R<sup>8</sup> and R<sup>9</sup> independently represent hydrogen or (1-6C)alkyl.

25 7. A compound accordingly to any one of the preceding claims wherein R<sup>1</sup> and R<sup>2</sup> are both hydrogen or R<sup>1</sup> is hydrogen or (1-6C)alkyl and R<sup>2</sup> is (1-6C)alkyl

wherein (1-6Calkyl) is optionally substituted by hydroxy, amino, mono(1-6C)alkylamino or di(1-6C)alkylamino, carbamoyl, (1-6C)alkoxy, (1-6C)alkoxy(1-6C)alkoxy, -N(R<sup>d</sup>)C(O)(1-6C)alkyl in which R<sup>d</sup> is hydrogen or (1-6C)alkyl, aryl (particularly phenyl), a saturated or partially saturated 3 to 7 30 membered heterocyclic ring or a 5 or 6 membered heteroaryl ring; wherein the (1-6C)alkoxy, mono(1-6C)alkylamino and -N(R<sup>d</sup>)C(O)(1-6C)alkyl groups are optionally substituted by hydroxy;

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wherein an aryl ring, a saturated or partially saturated 3 to 7 membered heterocyclic ring or a 5 or 6 membered heteroaryl ring is optionally substituted by (1-4C)alkyl, (1-4C)alkoxy or -C(O)CH<sub>2</sub>Y wherein Y is selected from hydroxy or di(1-6C)alkylamino.

5

8. A compound accordingly to any one of the preceding claims wherein R<sup>3</sup> and R<sup>4</sup> are both hydrogen.

9. A compound accordingly to any one of the preceding claims wherein R<sup>6</sup> is independently selected from halo, cyano, oxo, (3-7C)cycloalkyl, a saturated 3 to 7 membered heterocyclic ring (optionally substituted by (1-4C)alkyl), -N(R<sup>c</sup>)C(O)(1-6C)alkyl wherein R<sup>c</sup> is hydrogen or (1-6C)alkyl (particularly (1-4C)alkyl), (1-6C)alkyl (optionally substituted by up to three groups independently selected from halo) or (1-6C)alkoxy and m is selected from 1 or 2.

15

10. A compound according to Claim 1 which is any one or more of examples 1 to 152 or a salt thereof.

11. A pharmaceutical composition which comprises a compound of the Formula I, or a pharmaceutically acceptable salt thereof, as defined in claims 1 to 10 in association with a pharmaceutically acceptable diluent or carrier.

20. 12. A compound of the Formula I, or a pharmaceutically acceptable salt thereof, as defined in claims 1 to 10, for use as a medicament.

25

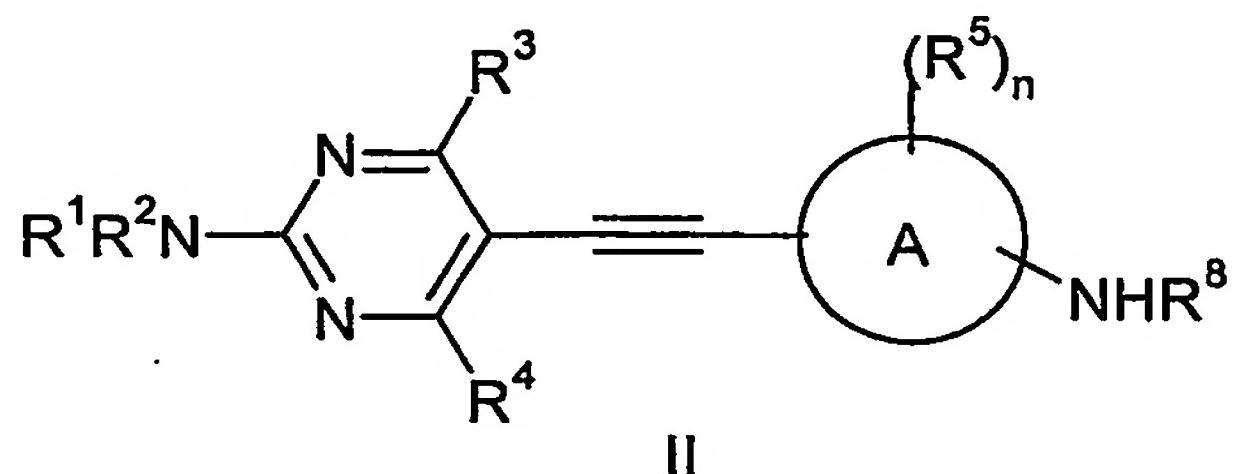
13. Use of a compound of the Formula I, or a pharmaceutically acceptable salt thereof, as defined in claims 1 to 10, in the manufacture of a medicament for use as a Tie2 receptor tyrosine kinase inhibitor in a warm-blooded animal such as man.

30 14. Use of a compound of the Formula I, or a pharmaceutically acceptable salt thereof, as defined in claims 1 to 10, in the manufacture of a medicament for use in the production of an anti-angiogenic effect in a warm-blooded animal such as man.

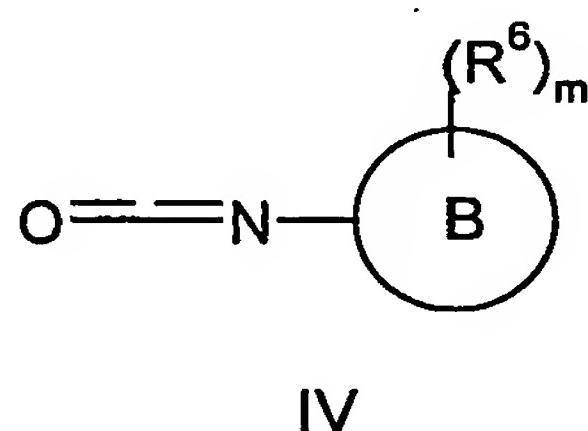
-171-

15. A process for preparing a compound of formula I, or salt thereof, as defined in Claim 1, or a pharmaceutically acceptable salt thereof (wherein  $R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}$ , L, ring A and ring B, n and m are, unless otherwise specified, as defined in Claim 1) comprising:

- 5 (a) For compounds of the formula I wherein L is  $-N(R^8)C(O)N(H)-$ , the reaction of a compound of the formula II:

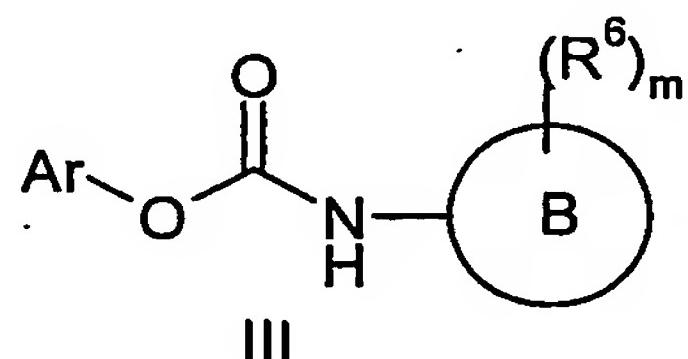


10 wherein  $R^1, R^2, R^3, R^4, R^5, R^8, n$  and A have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an isocyanate of the formula IV:



wherein  $R^6, m$  and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

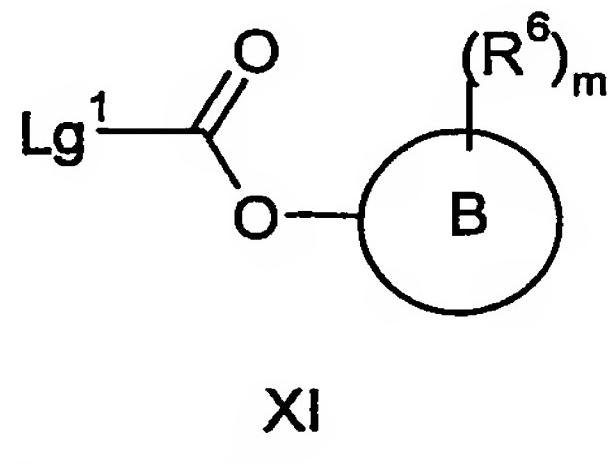
- 15 (b) For compounds of the formula I wherein L is  $-N(R^8)C(O)N(H)-$ , the reaction of a compound of the formula II as defined above with an aryl carbamate of the formula III:



20 wherein Ar is a suitable aryl group, for example phenyl, and  $R^6, m$  and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

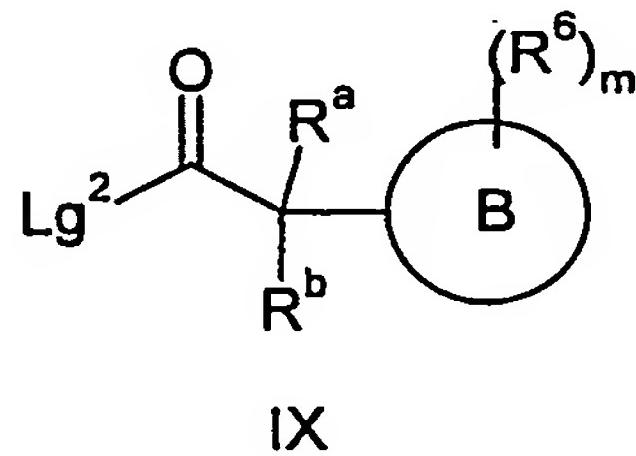
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- (c) For compounds of the formula I wherein L is  $N(R^8)C(O)-O-$ , the reaction of a compound of the formula II as defined above with a compound of the formula XI:



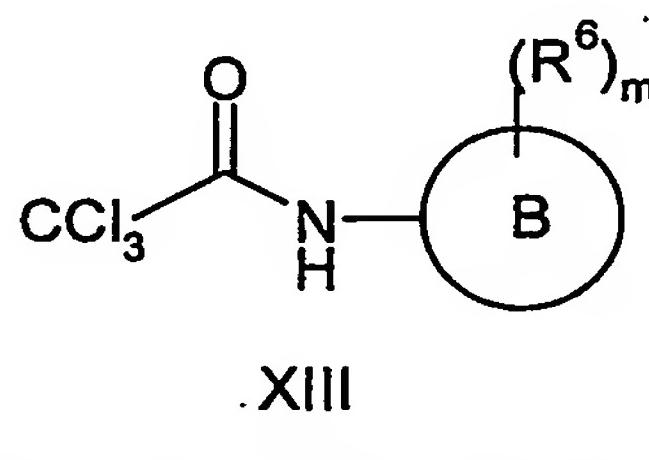
wherein Lg<sup>1</sup> is a suitable displaceable group for example halogeno (such as fluoro, chloro or bromo) and R<sup>6</sup>, m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

- (d) For compounds of the formula I wherein L is  $N(R^8)C(O)C(R^aR^b)$ , the reaction of a compound of the formula II as defined above with a compound of the formula IX:



wherein Lg<sup>2</sup> is a suitable displaceable group for example hydroxy, halogeno (such as fluoro, chloro or bromo),  $R^x-C(O)-O-$  or  $R^x-O-$  (wherein R<sup>x</sup> is a suitable alkyl or aryl group) and R<sup>6</sup>, R<sup>a</sup>, R<sup>b</sup>, m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

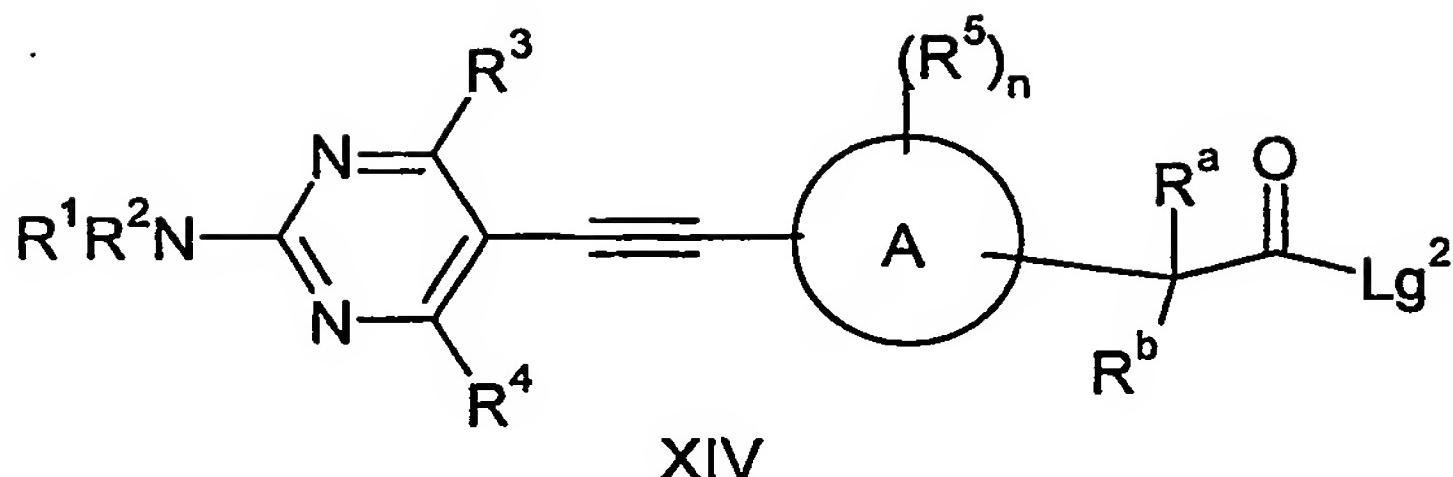
- (e) For compounds of the formula I wherein L is  $-N(R^8)C(O)N(H)-$ , the reaction of a compound of the formula II as defined above with a trichloroacetylamine of the formula XIII:



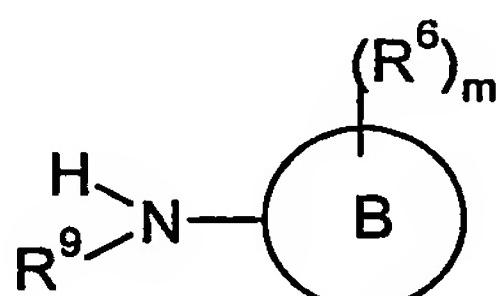
wherein R<sup>6</sup>, m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

- (f) For compounds of the formula I wherein L is  $-C(R^aR^b)C(O)N(R^9)-$ , the reaction of a compound of the formula XIV:

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wherein  $Lg^2$  is a suitable displaceable group as described above and  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^a$ ,  $R^b$ ,  $n$  and  $A$  have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an amine of the formula XV:

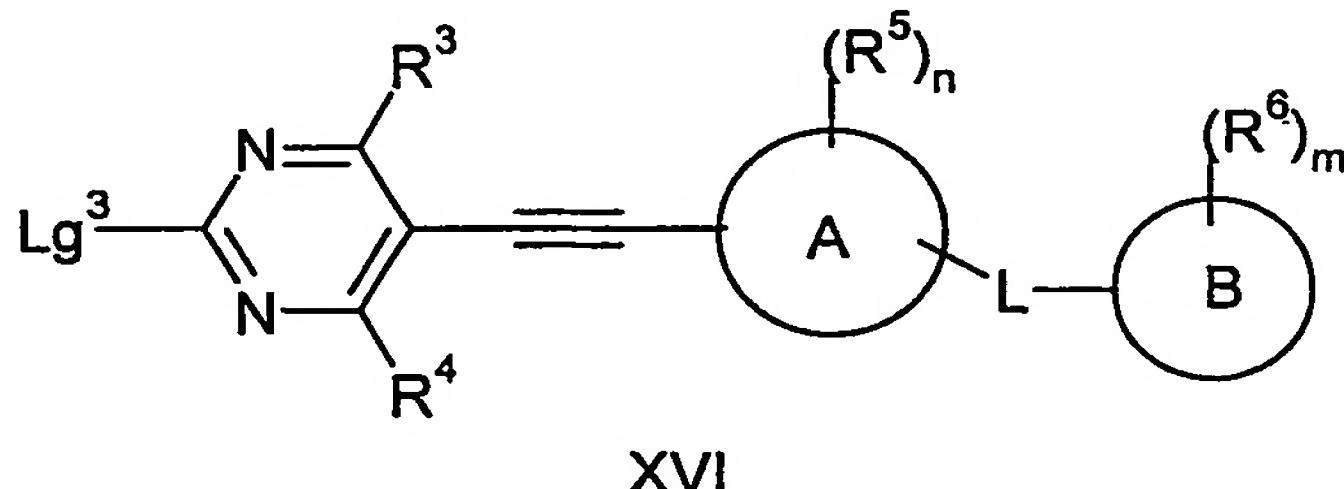


XV

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wherein  $R^6$ ,  $R^9$ ,  $m$  and  $B$  have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

- (g) The reaction of a compound of the formula XVI:

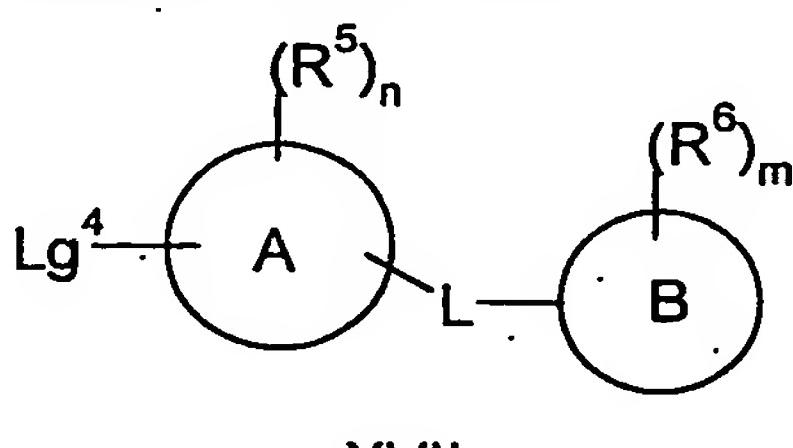


10

wherein  $Lg^3$  is a suitable displaceable group for example halogeno (such as fluoro, chloro, bromo or iodo), methyl sulfonyl, methylthio or aryloxy (such as phenoxy) and  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $n$ ,  $m$ ,  $A$ ,  $B$  and  $L$  have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an amine of the formula  $HNR^1R^2$ , wherein  $R^1$  and  $R^2$  have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

15

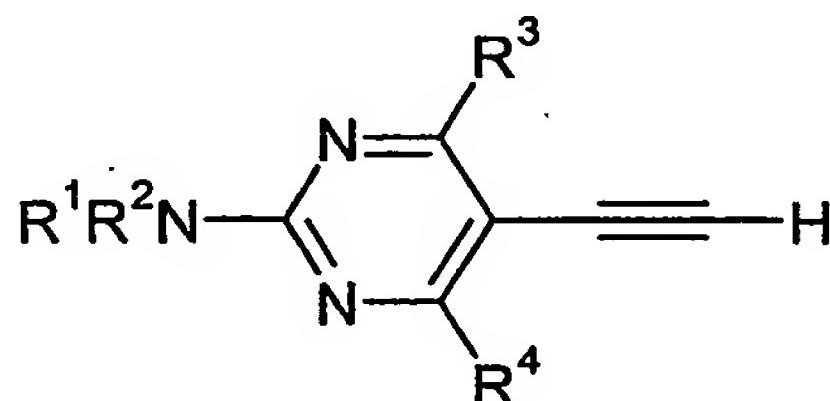
- (h) The reaction of a compound of the formula XVII:



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wherein  $Lg^4$  is a suitable displaceable group for example halogeno (such as chloro, bromo or iodo) or a sulfonyloxy group (such as trifluoromethylsulfonyloxy) and  $R^5$ ,  $R^6$ , n, m, A, B and L have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an alkyne of the formula XVIII:

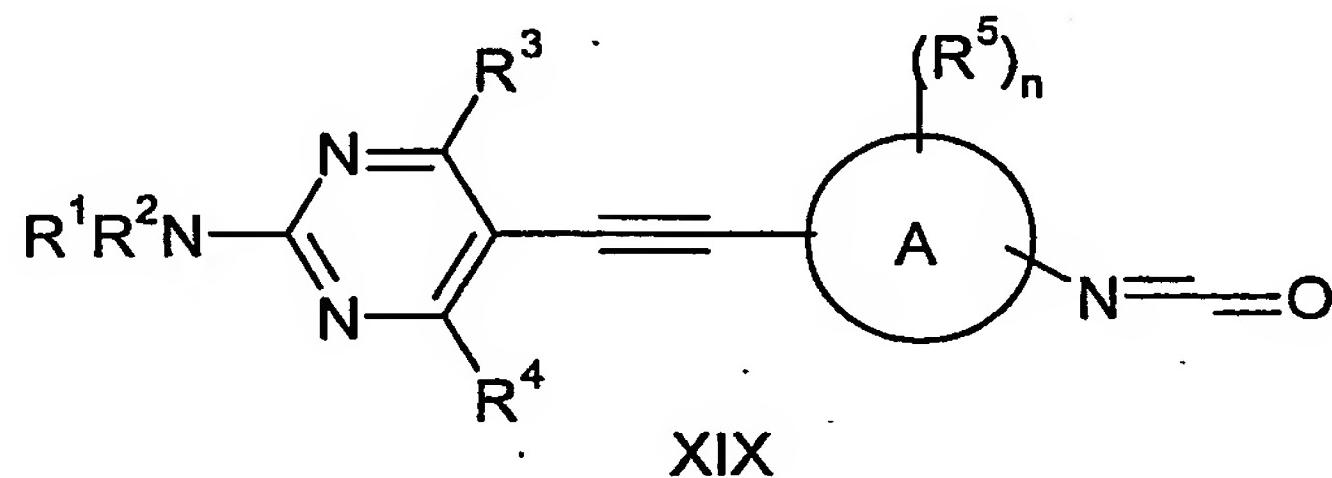
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XVIII

wherein  $R^1$ ,  $R^2$ ,  $R^3$  and  $R^4$  have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

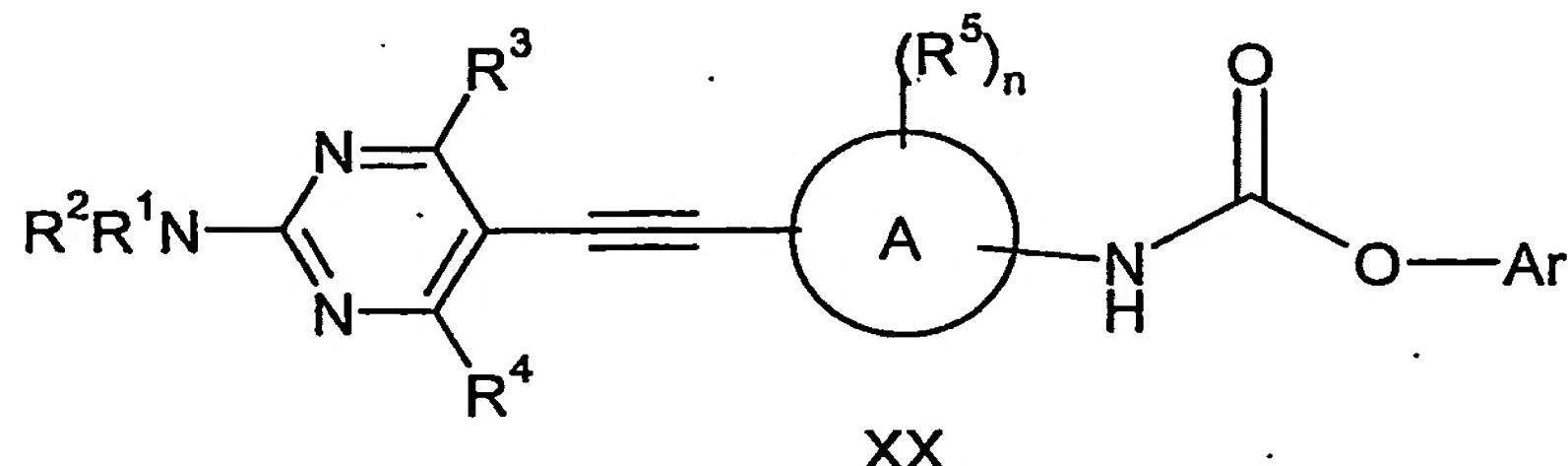
- 10 (i) For compounds of the formula I wherein L is  $-N(H)C(O)N(R^9)-$ , the reaction of an isocyanate of the formula XIX:



XIX

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , n and A have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an amine of the formula XV as defined above; or

- 15 (j) For compounds of the formula I wherein L is  $-N(H)C(O)N(R^9)-$ , the reaction of a compound of the formula XX:



XX

wherein Ar is a suitable aryl group, for example phenyl, and  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , n and A have any of the meanings defined hereinbefore except that any functional

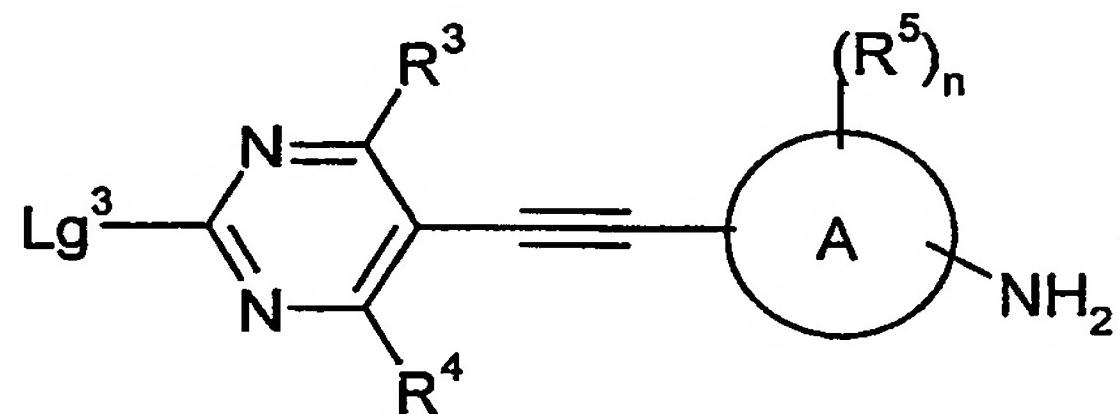
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group is protected if necessary, with an amine of the formula XV as defined above.

and thereafter if necessary:

- i) converting a compound of the Formula (I) into another compound of the Formula (I);  
5      ii) removing any protecting groups;  
      iii) forming a salt.

16. A compound selected from Formulae II, XIV, XVI, XIX and XX as defined in Claim 15 or a compound of Formula VIc:



10

VIc

or salt thereof, wherein  $Lg^3$ ,  $R^3$ ,  $R^4$ ,  $R^5$  and n are as defined in Claim 15.